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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/698,589	10/27/2000	Liliana Tejidor	9250.7	5412

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	8

DATE MAILED: 03/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/698,589	TEJIDOR ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) *52-82 and 95-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-51 and 83-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-100* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Restriction/Election

1. Applicant's election of Group 1, claims 1-51 and 83-94, with traverse, filed 1/18/02 in Paper No.7 is acknowledged. Claims 1-100 are pending. Claims 1-51 and 83-94 are under examination.

Applicant argues that while the two inventions in the restriction requirement are distinct, they are so related that a search of one invention would encompass the search for the other.

In response, restriction requirements are set forth for reasons of patentable distinction between each independent invention. The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. Further, while searches would be expected to overlap, there is no reason to expect the searches to be coextensive. The requirement is still deemed proper and is therefore made FINAL for reasons of record.

Drawings

2. The drawings in this application are objected to by the Draftsperson (see PTO-948 attached). Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New formal drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

C. Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-51 and 83-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in reciting, "capable of allowing assessment of the hemostatic potential" because it fails to recite a positive limitation in the claim.

Claim 5 is indefinite in reciting, "capable of" because it fails to recite a positive limitation in the claim. See also claim 6.

Claim 9 lacks antecedent support in reciting, "the phospholipid mixture".

In claims 9, "comprise" should be "comprises".

Claim 12 recites improper Markush language in reciting, "divalent metal cation selected from". Change to "divalent metal cation selected from the group consisting of" for proper Markush language.

Regarding claim 17, "and/or " renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "and/or"), thereby rendering the scope of the claim unascertainable.

Claim 31 is indefinite in reciting, "capable of" because it fails to recite a positive limitation in the claim. See also claim 32.

Claim 35 lacks antecedent support in reciting, "the phospholipid mixture".

In claims 35, "comprise" should be "comprises".

Claim 37 recites improper Markush language in reciting, "divalent metal cation selected from". Change to "divalent metal cation selected from the group consisting of" for proper Markush language.

Regarding claim 42, "and/or " renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "and/or"), thereby rendering the scope of the claim unascertainable.

Claim 83 is indefinite because it is unclear what Applicant intends to encompass in reciting, "heparin-like molecules".

Claim 88 is indefinite in reciting, "capable of" because it fails to recite a positive limitation in the claim.

Claim 88 lacks antecedent support in reciting, "the initiation phase".

Claim 89 is indefinite because it is unclear what Applicant intends to encompass in reciting, "heparin-like molecules".

Claim 94 is indefinite in reciting, "capable of" because it fails to recite a positive limitation in the claim.

Claim 94 lacks antecedent support in reciting, "the initiation phase".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 1, 3-6, 11, 14-16, and 88 are rejected under 35 U.S.C. 102(e) as being anticipated by Spillert et al. (US 6,245,573).

Spillert et al. disclose a reagent for use in assessing coagulant activity, i.e. hypocoagulation or hypercoagulation, in plasma or whole blood by measuring stasis

(clotting) in the presence of metal salts (see column 1). The reagent comprises metal salts in aqueous solution and other modulators of the clotting process including tissue factor (a coagulation activator) and thrombomodulin (a protein C activator) (see column 6, line 43 to column 7, line 53).

5. Claims 1-8, 11-13, 17, 85, and 87-88 are rejected under 35 U.S.C. 102(b) as being by anticipated by Hawkins et al. (US 5,625,036).

Hawkins et al. disclose a reagent for use in determining coagulation function, i.e. hypocoagulation or hypercoagulation, in order to diagnose coagulation function in patients. The reagent comprises recombinant or purified natural human tissue factor, phospholipids of natural or synthetic origin, calcium, i.e. metal salt, buffer composition, and stabilizers such as glycine or dextrans (see column 2, line 66 to column 3, line 29). The phospholipid composition contains phosphatidylcholine : phosphatidylserine in the ratio of 70:30 (see column 4, lines 33-50).

6. Claims 1-3, 5-10, 14-16, and 85-88 are rejected under 35 U.S.C. 102(b) as being by anticipated by Smirnov et al. (US 5,472,852).

Smirnov et al. disclose a reagent for use in determining the propensity of a patient for thrombotic disease. The reagent comprises a phospholipid component comprising effective amounts of phosphatidylethanolamine (PE), phosphatidylserine (PS), and phosphatidylcholine (PC), Tissue Factor, activated Protein C. Preferably the ratio therebetween is 10-50% PE, 5-50% PS, and the rest PC (see Summary, column 4,

lines 45-62 and column 6, lines 39-45). The phospholipid vesicles are formed by sonication, dialysis, etc. (see column 4, line 63 to column 5, line 26).

7. Claims 1-2, 4-7, 12-17, and 83-88 are rejected under 35 U.S.C. 102(b) as being by anticipated by KRAUS et al. (2,2252,983)

Kraus et al. disclose a reagent for use in determining coagulation potential in a sample for diagnosis of thrombotic disease. The reagent comprises exogenous thrombomodulin to activate protein C, thromboplastin (coagulation activator), phospholipids, calcium ions (see page 14, lines 15-30page 15, lines 13-29). Other additional components such as wash solution, buffers, and stabilizers are included in the reagent to optimize the coagulation test (see page 15, lines 13-29). Thrombomodulin are heparin or heparin-like molecules whose interference can be eliminated by degradation or neutralization by enzymes (see page 16, lines 20-29). Phosphatidylethanolamine which is important in the activity of Protein C can be metered in, as required, to relipidate thrombomodulin (see page 19, lines 1-11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 18-20, 25-34, 36-51, 91, and 93-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spillert et al. (US 6,245,573) or Hawkins et al. (US 5,625,036).

Spillert et al. disclose a reagent for use in assessing coagulant activity, i.e. hypocoagulation or hypercoagulation, in plasma or whole blood by measuring stasis (clotting) in the presence of metal salts (see column 1). The reagent comprises metal salts in aqueous solution and other modulators of the clotting process including tissue factor (a coagulation activator) and thrombomodulin (a protein C activator) (see column 6, line 43 to column 7, line 53).

Hawkins et al. disclose a reagent for use in determining coagulation function, i.e. hypocoagulation or hypercoagulation, in order to diagnose coagulation function in patients. The reagent comprises recombinant or purified natural human tissue factor, phospholipids of natural or synthetic origin, calcium, i.e. metal salt, buffer composition, and stabilizers such as glycine or dextrans (see column 2, line 66 to column 3, line 29).

The phospholipid composition contains phosphatidylcholine : phosphatidylserine in the ratio of 70:30 (see column 4, lines 33-50).

Spillert et al. and Hawkins et al. differ in failing to disclose the concentrations of tissue factor, thrombomodulin, phospholipids, metal cations or salts, and buffers/stabilizers such as recited in claims 18-20, 25-27, 29, and 43-51.

However, it is maintained that concentrations of different compositions or components in coagulation reagents such as tissue factor, thrombomodulin, phospholipids, metal cations or salts, and buffers/stabilizers recited in claims 18-20, 25-27, 29, and 43-51, are all result effective variables which the Spillert and Hawkins have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). Since Applicant has not disclosed that the specific limitations recited in instant claims 18-20, 25-27, 29, and 43-51 encompassing various concentration values are for any particular purpose or solve any stated problem and the prior art teaches that different compositions in coagulation reagents often vary according to the sample being analyzed and various specific concentrations taught by prior art appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the reagents and methods disclosed by the prior art by normal optimization procedures.

9. Claims 21-22, 27-29, 31-36, 43-47, and 91-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smirnov et al. (US 5,472,852).

Smirnov et al. disclose a reagent for use in determining the propensity of a patient for thrombotic disease. The reagent comprises a phospholipid component comprising effective amounts of phosphatidylethanolamine (PE), phosphatidylserine (PS), and phosphatidylcholine (PC), Tissue Factor, activated Protein C. Preferably the ratio therebetween is 10-50% PE, 5-50% PS, and the rest PC (see Summary, column 4, lines 45-62 and column 6, lines 39-45). The phospholipid vesicles are formed by sonication, dialysis, etc. (see column 4, line 63 to column 5, line 26).

Smirnov et al. differ in failing to disclose the concentrations of the tissue factor and phospholipids such as recited in claims 21-22, 27, 29, and 43-47.

However, it is maintained that concentrations of different compositions or components in coagulation reagents such as tissue factor and phospholipids recited in claims 21-22, 27, 29, and 43-47, are all result effective variables which the Smirnov has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the

specific limitations recited in instant claims 21-22, 27, 29, and 43-47 encompassing various concentration values are for any particular purpose or solve any stated problem and the prior art teaches that different compositions in coagulation reagents often vary according to the sample being analyzed and various specific concentrations taught by prior art appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the reagents and methods disclosed by the prior art by normal optimization procedures.

10. Claims 23-24, 27-28, 30-33, 37-42, 46-47, 46-51, 89-91, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus et al. (2,2252,983).

Kraus et al. disclose a reagent for use in determining coagulation potential in a sample for diagnosis of thrombotic disease. The reagent comprises exogenous thrombomodulin to activate protein C, thromboplastin (coagulation activator), phospholipids, calcium ions (see page 14, lines 15-30page 15, lines 13-29). Other additional components such as wash solution, buffers, and stabilizers are included in the reagent to optimize the coagulation test (see page 15, lines 13-29). Thrombomodulin are heparin or heparin-like molecules whose interference can be eliminated by degradation or neutralization by enzymes (see page 16, lines 20-29). Phosphatidylethanolamine which is important in the activity of Protein C can be metered in, as required, to relipidate thrombomodulin (see page 19, lines 1-11).

Kraus et al. differ in failing to disclose the concentrations of the tissue factor and phospholipids such as recited in claims 23-24, 27, 29, and 43-47.

However, it is maintained that concentrations of different compositions or components in coagulation reagents such as thromboplastin, thrombomodulin, phospholipids, metal cations or salts, and buffers/stabilizers recited in claims 23-24, 27, 29, and 43-47, are all result effective variables which the Kraus has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). Since Applicant has not disclosed that the specific limitations recited in instant claims 23-24, 27, 29, and 43-47 encompassing various concentration values are for any particular purpose or solve any stated problem and the prior art teaches that different compositions in coagulation reagents often vary according to the sample being analyzed and various specific concentrations taught by prior art appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the reagents and methods disclosed by the prior art by normal optimization procedures.

11. No claims allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R Gabel whose telephone number is (703) 305-

9297. The examiner can normally be reached on Monday-Thursday 6:00 AM to 3:30 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
March 24, 2002

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/1641